* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:02:01 ON 24 OCT 2007

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:02:17 ON 24 OCT 2007

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STRUCTURE FILE UPDATES: 23 OCT 2007 HIGHEST RN 951288-30-5
DICTIONARY FILE UPDATES: 23 OCT 2007 HIGHEST RN 951288-30-5

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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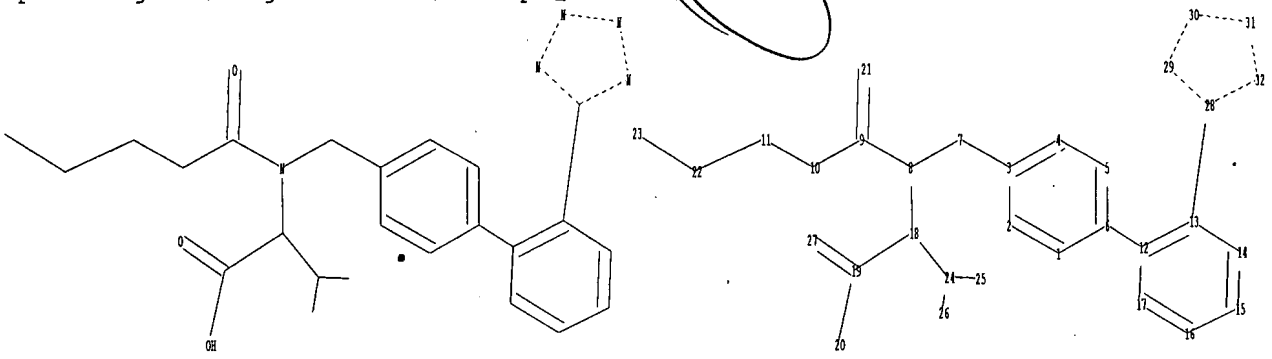
http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10528323.str



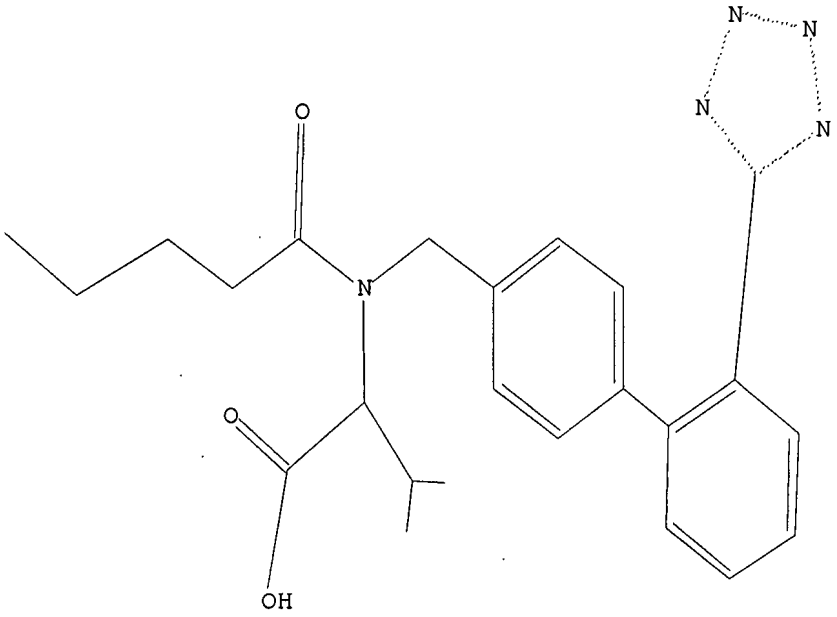
chain nodes :
7 8 9 10 11 18 19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 12 13 14 15 16 17 28 29 30 31 32
chain bonds :
3-7 6-12 7-8 8-9 8-18 9-10 9-21 10-11 11-22 13-28 18-19 18-24 19-20 19-27 22-23 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 28-29 28-32 29-30 30-31 31-32
exact/norm bonds :

7-8 8-9 8-18 9-21 28-29 28-32 29-30 30-31 31-32
exact bonds :
3-7 6-12 9-10 10-11 11-22 13-28 18-19 18-24 22-23 24-25 24-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 19-20
19-27

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
 11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom

L1   STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:02:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   28 TO ITERATE

100.0% PROCESSED   28 ITERATIONS   5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 243 TO   877
PROJECTED ANSWERS: 5 TO   234

L2   5 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 14:02:37 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 613 TO ITERATE

100.0% PROCESSED 613 ITERATIONS 100 ANSWERS
SEARCH TIME: 00.00.01

L3 100 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'CAPLUS' ENTERED AT 14:02:39 ON 24 OCT 2007
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FILE COVERS 1907 - 24 Oct 2007 VOL 147 ISS 18
FILE LAST UPDATED: 23 Oct 2007 (20071023/ED)

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http://www.cas.org/infopolicy.html

=> s l3
L4 1348 L3

=> fil reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.47 172.78

FILE 'REGISTRY' ENTERED AT 14:02:51 ON 24 OCT 2007
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DICTIONARY FILE UPDATES: 23 OCT 2007 HIGHEST RN 951288-30-5

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and

predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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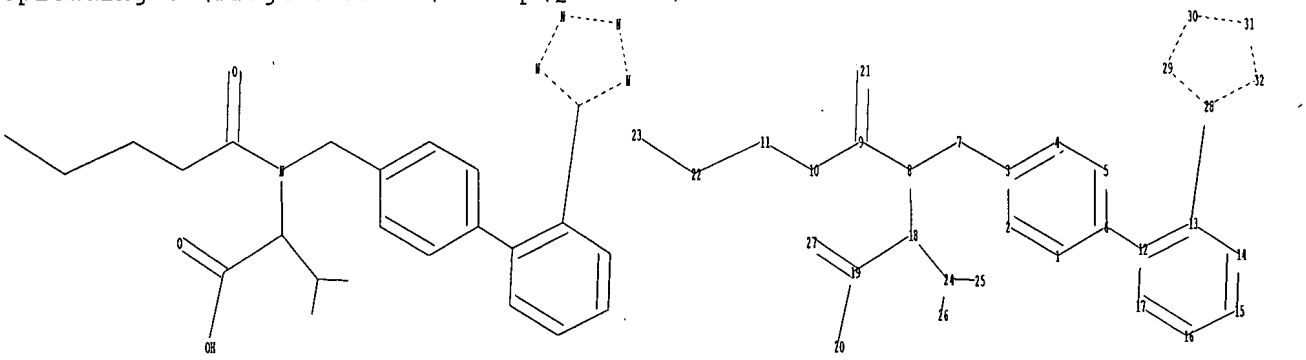
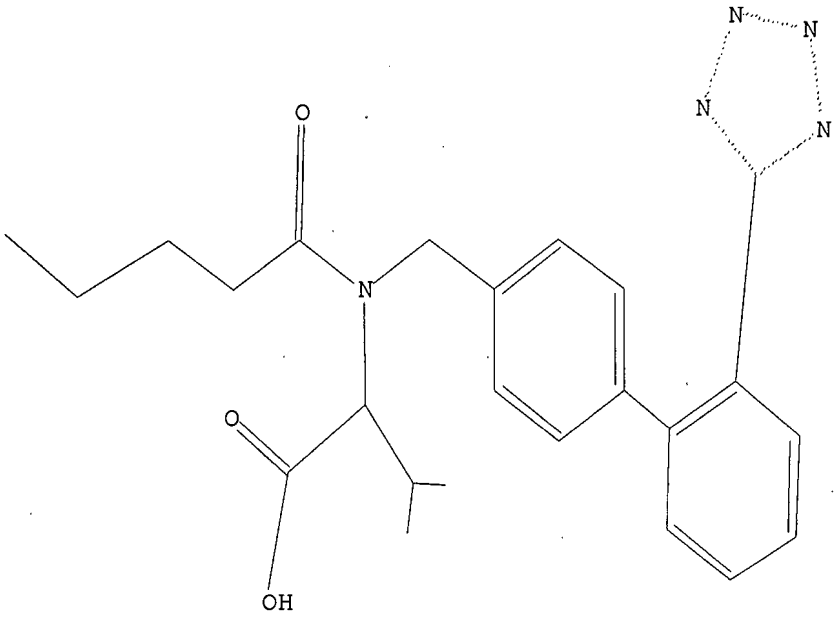


chain nodes :
7 8 9 10 11 18 19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 12 13 14 15 16 17 28 29 30 31 32
chain bonds :
3-7 6-12 7-8 8-9 8-18 9-10 9-21 10-11 11-22 13-28 18-19 18-24 19-20
19-27 22-23 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 28-29
28-32 29-30 30-31 31-32
exact/norm bonds :
7-8 8-9 8-18 9-21 28-29 28-32 29-30 30-31 31-32
exact bonds :
3-7 6-12 9-10 10-11 11-22 13-28 18-19 18-24 22-23 24-25 24-26
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17 19-20
19-27

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:Atom 29:Atom 30:Atom 31:Atom 32:Atom

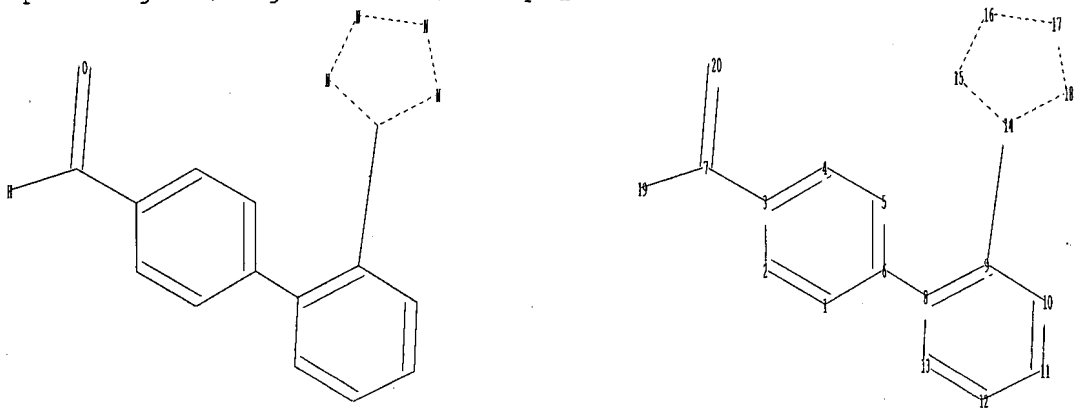
L5 STRUCTURE UPLOADED

=> d
L5 HAS NO ANSWERS
L5 STR



Structure attributes must be viewed using STN Express query preparation.

=>
Uploading C:\Program Files\Stnexp\Queries\10528323b.str



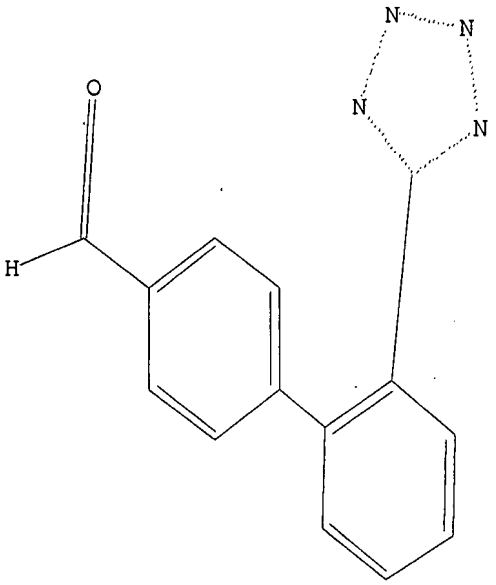
chain nodes :
7 19 20
ring nodes :
1 2 3 4 5 6 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
3-7 6-8 7-19 7-20 9-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13 14-15 14-18
15-16 16-17 17-18
exact/norm bonds :
7-20 14-15 14-18 15-16 16-17 17-18
exact bonds :
3-7 6-8 7-19 9-14
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-13 9-10 10-11 11-12 12-13

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS

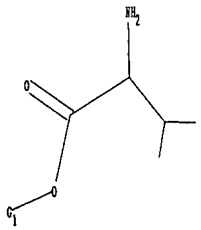
L6 STRUCTURE UPLOADED

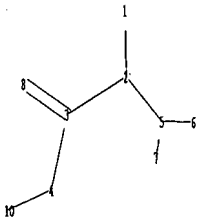
=> d
L6 HAS NO ANSWERS
L6 STR



Structure attributes must be viewed using STN Express query preparation.

=>
Uploading C:\Program Files\Stnexp\Queries\10528323c.str





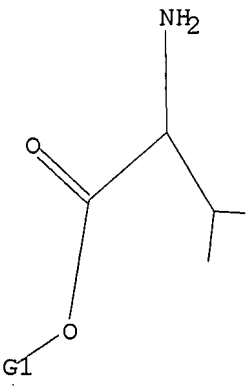
chain nodes :
1 2 3 4 5 6 7 8 10
chain bonds :
1-2 2-3 2-5 3-4 3-8 4-10 5-6 5-7
exact/norm bonds :
1-2 3-4 3-8 4-10
exact bonds :
2-3 2-5 5-6 5-7

G1:H,O

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 10:CLASS

L7 STRUCTURE UPLOADED

=> d
L7 HAS NO ANSWERS
L7 STR



G1 H,O

Structure attributes must be viewed using STN Express query preparation.

=> s l5 and l6 and l7
SAMPLE SEARCH INITIATED 14:05:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 33 TO 447
PROJECTED ANSWERS: 0 TO 0

L8 0 SEA SSS SAM L5 AND L6 AND L7

=> s l5 and l6 and l7 full
FULL SEARCH INITIATED 14:06:04 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 274 TO ITERATE

100.0% PROCESSED 274 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L9 0 SEA SSS FUL L5 AND L6 AND L7

=> s l5 and l6
SAMPLE SEARCH INITIATED 14:06:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L5 AND L6

=> s l5 and l6 full
FULL SEARCH INITIATED 14:06:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 25 TO ITERATE

100.0% PROCESSED 25 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

```
L11           0 SEA SSS FUL L5 AND L6

=> s l6
SAMPLE SEARCH INITIATED 14:06:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      837 TO ITERATE

100.0% PROCESSED      837 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        15005 TO    18475
PROJECTED ANSWERS:               1 TO       80

L12           1 SEA SSS SAM L6

=> s l6 and l7
SAMPLE SEARCH INITIATED 14:06:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       36 TO ITERATE

100.0% PROCESSED       36 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          360 TO     1080
PROJECTED ANSWERS:               0 TO        0

L13           0 SEA SSS SAM L6 AND L7

=> s l6 and l7 full
FULL SEARCH INITIATED 14:06:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      666 TO ITERATE

100.0% PROCESSED      666 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L14           0 SEA SSS FUL L6 AND L7

=> s l5
SAMPLE SEARCH INITIATED 14:06:40 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       28 TO ITERATE

100.0% PROCESSED       28 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          243 TO      877
PROJECTED ANSWERS:               5 TO      234

L15           5 SEA SSS SAM L5

=> s l5 full
FULL SEARCH INITIATED 14:06:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      613 TO ITERATE

100.0% PROCESSED      613 ITERATIONS                              100 ANSWERS
SEARCH TIME: 00.00.01

L16         100 SEA SSS FUL L5

=> s l6
```

```
SAMPLE SEARCH INITIATED 14:06:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      837 TO ITERATE

100.0% PROCESSED      837 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        15005 TO    18475
PROJECTED ANSWERS:               1 TO       80

L17           1 SEA SSS SAM L6

=> s l6 full
FULL SEARCH INITIATED 14:06:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    16091 TO ITERATE

100.0% PROCESSED    16091 ITERATIONS                                12 ANSWERS
SEARCH TIME: 00.00.01

L18          12 SEA SSS FUL L6

=> s l7 full
FULL SEARCH INITIATED 14:06:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  1321324 TO ITERATE

 75.7% PROCESSED  1000000 ITERATIONS                             1160 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.07

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:     1321324 TO  1321324
PROJECTED ANSWERS:           1415 TO     1649

L19        1160 SEA SSS FUL L7

=> s l16 and l18 and l19
L20          0 L16 AND L18 AND L19

=> s l6 full
FULL SEARCH INITIATED 14:07:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    16091 TO ITERATE

100.0% PROCESSED    16091 ITERATIONS                                12 ANSWERS
SEARCH TIME: 00.00.01

L21          12 SEA SSS FUL L6

=> fil caplus
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
FULL ESTIMATED COST                          1205.15    1377.93

FILE 'CAPLUS' ENTERED AT 14:07:22 ON 24 OCT 2007
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FILE COVERS 1907 - 24 Oct 2007 VOL 147 ISS 18
FILE LAST UPDATED: 23 Oct 2007 (20071023/ED)

=> s l21
L22 22 L21

=> d ibib abs hitstr tot
THE ESTIMATED COST FOR THIS REQUEST IS 115.94 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

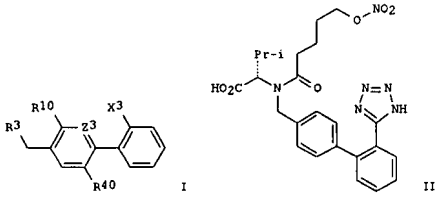
L22 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:146833 CAPLUS
DOCUMENT NUMBER: 146:229356
TITLE: Nitric oxide enhancing angiotensin II antagonist compounds, and their preparation, compositions, and methods of use
INVENTOR(S): Garvey, David S.; Cai, Xiong; Fang, Xinqin; Ranatunge, Ramani R.; Wey, Shiow-Jyi; Zhai, Hai-Xiao
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 58pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007032533	A1	20070208	US 2006-499770	20060807
WO 2007019448	A2	20070215	WO 2006-US30733	20060807

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:		US 2005-706005P	P 20050808
		US 2005-706419P	P 20050809
		US 2005-748579P	P 20051209

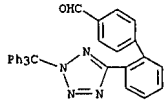
OTHER SOURCE(S): MARPAT 146:229356
GI



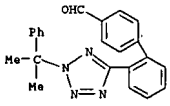
AB The invention describes compns. and kits comprising at least one nitric oxide enhancing angiotensin II antagonist compound of formula I, or pharmaceutically acceptable salts thereof, and compns. comprising at least one nitric oxide enhancing angiotensin II antagonist compd., and, optionally, at least one nitric oxide enhancing compd. and/or at least one therapeutic agent. Compds. of formula I wherein X3 is (un)substituted azole, (un)substituted sulfonylaminoxazole, (un)substituted aminosulfonyl, (un)substituted acyl, etc.; Y3 is (un)substituted azole, (un)substitute valine deriv., (un)substituted amide, etc.; Z3 is CH and N; R10 is F and H; R40 is H, lower alkyl, alkoxyalkyl, etc.; and their pharmaceutically acceptable salts thereof are claimed. The invention also provides methods for (a) treating cardiovascular diseases; (b) treating renovascular diseases; (c) treating diabetes; (d) treating diseases resulting from oxidative stress; (e) treating endothelial dysfunctions; (f) treating diseases caused by endothelial dysfunctions; (g) treating cirrhosis; (h) treating pre-eclampsia; (j) treating osteoporosis; (k) treating nephropathy; (l) treating peripheral vascular diseases; (m) treating portal hypertension (o) treating central nervous system disorders; (p) treating metabolic syndrome; and (q) treating hyperlipidemia. The nitric oxide enhancing angiotensin II antagonist compds. comprise at least one nitric oxide enhancing group linked to the angiotensin II antagonist compd. through one or more sites such as carbon, oxygen and/or nitrogen via a bond or moiety that cannot be hydrolyzed. Example compd. II was prepd. by redn. of 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-carboxylic acid Me ester; the resulting 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methanol underwent oxidn. to give 2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-carboxaldehyde, which underwent condensation with L-valine tert-Bu ester hydrochloride to give (E)-N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methylene]-L-valine tert-Bu ester, which underwent redn. to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-L-valine tert-Bu ester, which underwent amidation with 5-(nitrooxy)pentanoic acid to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-N-[5-(nitrooxy)-1-oxopentyl]-L-valine tert-Bu ester, which underwent hydrolysis to give N-[2'[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-[1,1'-biphenyl]-4-methyl]-N-[5-(nitrooxy)-1-oxopentyl]-L-valine, which underwent detritylation to give compd. II. All the invention compds. were evaluated for their AT1 inhibitory activity. From the assay, it was detd. that compd. II exhibited an IC50 value of 19 nM and 86% inhibition at 100 nM.

IT 138804-35-0P 165670-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzimidazole-tetrazole-nitric oxide compds.
as enhancing angiotensin II antagonist compds. and their use in treatment of disease)

RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



RN 165670-62-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



L22 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:58763 CAPLUS
DOCUMENT NUMBER: 146:163123
TITLE: Preparation of metal salts of 2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-carboxaldehyde
INVENTOR(S): Seedmeier, Gottfried; Grimler, Dominique
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 21pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007006531	A1	20070118	WO 2006-EP6730	20060710

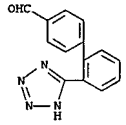
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:		GB 2005-14206	A 20050711

AB The invention relates to the preparation of 2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-carboxaldehyde (I) metal salts for use in the manufacture of blood pressure-lowering agents such as valsartan. Examples describe the preparation of the potassium, sodium, and lithium salts by treating I with alkali metal hydroxides in methanol solution

IT 151052-40-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of metal salts of tetrazolylbiphenylcarboxaldehyde as intermediates in synthesis of valsartan)

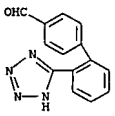
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



IT 920034-06-6P 920034-07-7P 920034-08-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of metal salts of tetrazolylbiphenylcarboxaldehyde as intermediates in synthesis of valsartan)

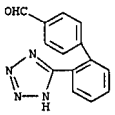
RN 920034-06-6 CAPLUS

L22 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)-, potassium salt (1:1) (CA INDEX NAME)



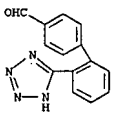
● K

RN 920034-07-7 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)-, sodium salt (1:1) (CA INDEX NAME)



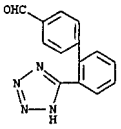
● Na

RN 920034-08-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)-, lithium salt (1:1) (CA INDEX NAME)



● Li

L22 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:921373 CAPLUS
DOCUMENT NUMBER: 143:367253
TITLE: Efficient, protection-free Suzuki-Miyaura synthesis of ortho-biphenyltetrazoles
AUTHOR(S): Cousaert, Nicolas; Toto, Patrick; Willand, Nicolas; Deprez, Benoit
CORPORATE SOURCE: Laboratoire de Chimie Generale et de Chimie Organique, Faculte des Sciences Pharmaceutiques et Biologiques, UMR 8525, Lille, F 59006, Fr.
SOURCE: Tetrahedron Letters (2005), 46(38), 6529-6532
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:367253
AB An efficient protocol is described for the Suzuki-Miyaura synthesis of ortho-biphenyltetrazoles from non-protected 2-bromophenyltetrazole and arylboronic acids. The optimized conditions were achieved using [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) as catalyst and Na2CO3 as base. A panel of structurally diverse arylboronic acids was used to demonstrate the scope of the coupling procedure.
IT 151052-40-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of o-biphenyltetrazoles by cross-coupling of (o-bromophenyl)tetrazole with arylboronates by protection-free Suzuki-Miyaura protocol)
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:823694 CAPLUS
DOCUMENT NUMBER: 143:229864
TITLE: A preparation of (1H-tetrazol-5-yl)-biphenyl derivatives, useful as intermediates for the manufacture of angiotensin II receptor antagonists
INVENTOR(S): Krell, Christoph; Hirt, Hans
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075462	A1	20050818	WO 2005-EP978	20050201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005211500	A1	20050818	AU 2005-211500	20050201
CA 2553246	A1	20050818	CA 2005-2553246	20050201
EP 1716140	A1	20061102	EP 2005-707117	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
CN 1914197	A	20070214	CN 2005-80003794	20050201
BR 2005007352	A	20070703	BR 2005-7352	20050201
JP 2007519684	T	20070719	JP 2006-550140	20050201
MX 2006PA08678	A	20061009	MX 2006-PA8678	20060801
IN 2006CN02815	A	20070608	IN 2006-CN2815	20060801
US 2007129413	A1	20070607	US 2006-588169	20060802
NO 2006003920	A	20061030	NO 2006-3920	20060901

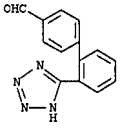
PRIORITY APPLN. INFO.:
GB 2004-2262 A 20040202
WO 2005-EP978 W 20050201

OTHER SOURCE(S): CASREACT 143:229864; MARPAT 143:229864
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of (1H-tetrazol-5-yl)-biphenyl derivs.
of formula I [wherein: Y is a tetrazole protecting group; R1 and R2 are independently alkyl or combined together form alkylene], useful as intermediates for the manufacture of angiotensin II receptor antagonists (no data). For instance, (1H-tetrazol-5-yl)-biphenyl derivative II was prepared via
NiCl2(dppp)-catalyzed coupling of 4-([1,3]dioxan-2-yl)phenylmagnesium bromide with (chlorophenyl)tetrazole derivative III.
IT 151052-40-3P

L22 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (1H-tetrazol-5-yl)-biphenyl derivs. useful as intermediates for the manuf. of angiotensin II receptor antagonists)
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)

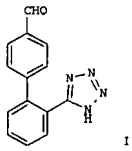


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238970 CAPLUS
DOCUMENT NUMBER: 142:316843
TITLE: Process for producing 2'-(1H-tetrazol-5-yl)-biphenyl-4-carbaldehyde
INVENTOR(S): Itaya, Nobushige; Matsui, Kozo; Ohtani, Yutaka; Ueno, Hiroki; Kaneko, Toshikazu
PATENT ASSIGNEE(S): Sumitomo Chemical Company, Limited, Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005023785	A1	20050317	WO 2004-JP13014	20040901
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2005082496	A	20050331	JP 2003-313325	20030904
EP 1666471	A1	20060607	EP 2004-772886	20040901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007072923	A1	20070329	US 2006-595122	20060524
PRIORITY APPLN. INFO.:			JP 2003-313325 A	20030904
			WO 2004-JP13014 W	20040901

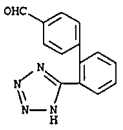
GI



I

AB A process for producing 2'-(1H-tetrazol-5-yl)-biphenyl-4-carboxaldehyde (I) comprises reacting 2'-cyanobiphenyl-4-carbaldehyde (II) with an azide salt. A process for producing high-purity crystals of I comprises reacting II with an azide salt to obtain crystals of I, dissolving the crystals in THF, and recrystg. the aldehyde to obtain high-purity crystals thereof. By the process, I crystals having a high purity and substantially free from 2'-(1H-tetrazol-5-yl)-biphenyl-4-carboxylic acid

L22 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(III), which are useful as an intermediate for medicines, e.g. an antihypertensive (angiotensin II inhibitor), can be produced in high yield through a small no. of steps. Thus, 400 g 2'-cyano-4-(bromomethyl)biphenyl was added to 1,000 g monochlorobenzene, followed by adding 812 g H2O, 412 g hexamethylenetetramine, and 618 g AcOH, and the resulting mixt. was heated at 90° with stirring for 9 h to give, after workup, 235.6 g II (77.3%). II (1,294 g) and 2,579 g Et3N.HCl were added to 8,510 g monochlorobenzene, followed by adding NaN3 1,218 g, and the resulting mixt. was heated at .apprx.110° with stirring, cooled to 10° when HPLC showed the area % of II.was ≤1%, treated with 12.64 kg THF and 4.79 kg H2O and then 5.745 kg 15% aq. NaNO2 soln., adjusted to pH 5.0±0.1 by adding 5.745 kg 17.5% aq. HCl soln., concd. under reduced pressure at 40-45 kPa and 35-45° by distg. away 12.2 kg solvent, and cooled to 0-5° at cooling rate of 10°/h, aged at the same temp. for 5 h, and filtered, to give after washing with 1,294 kg monochlorobenzene and drying under reduced pressure at ≤50°, 80.0% crude I (96.1% purity) contg. 0.73% III. Recrystn. of I from THF gave III (99.5% purity) which was free from III.
IT 151052-40-3P, 2'-(1H-Tetrazol-5-yl)-1,1'-biphenyl-4-carboxaldehyde
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(process for producing 2'-(1H-tetrazol-5-yl)-biphenyl-4-carboxaldehyde by cycloaddn. of 2'-cyanobiphenylcarboxaldehyde with sodium azide and recrystn. from THF)
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:141074 CAPLUS
DOCUMENT NUMBER: 142:240438
TITLE: A preparation of tetrazole derivatives via heterocyclization of nitriles with azides
INVENTOR(S): Sedelmeier, Gottfried
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

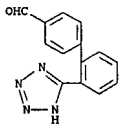
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014602	A1	20050217	WO 2004-EP7980	20040715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004263265	A1	20050217	AU 2004-263265	20040715
AU 2004263265	B2	20070906		
CA 2532175	A1	20050217	CA 2004-2532175	20040715
EP 1646636	A1	20060419	EP 2004-801815	20040715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004012558	A	20060919	BR 2004-12558	20040715
CN 1852908	A	20061025	CN 2004-80026438	20040715
IN 2006CN00155	A	20070629	IN 2006-CN155	20060112
MX 2006PA00561	A	20060330	MX 2006-PA561	20060113
NO 2006000729	A	20060404	NO 2006-729	20060215
US 2007043098	A1	20070222	US 2006-564337	20060811
PRIORITY APPLN. INFO.:			GB 2003-16546 A	20030715
			WO 2004-EP7980 W	20040715

OTHER SOURCE(S): CASREACT 142:240438; MARPAT 142:240438
GI

I

AB The invention relates to a preparation of tetrazole derivs. of formula I (R is organic residue) via heterocyclization of nitriles with azides. For instance, 5-(2-chlorophenyl)-1H-tetrazole was prepared via heterocyclization of 2-chlorobenzonitrile with sodium azide.
IT 151052-40-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

L22 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(prepn. of tetrazole derivs. via heterocyclization of azides with nitriles)
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267315 CAPLUS
DOCUMENT NUMBER: 140:287711
TITLE: Process for the manufacture of valsartan
INVENTOR(S): Denni-Dischert, Donatienne; Hirt, Hans; Neville, Dan; Seedmeier, Gottfried; Schnyder, Anita; Derrien, Nadine; Kaufmann, Daniel
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

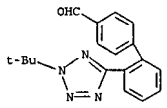
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026847	A1	20040401	WO 2003-EP10543	20030922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2502629	A1	20040401	CA 2003-2502629	20030922
AU 2003270241	A1	20040408	AU 2003-270241	20030922
AU 2003270241	B2	20070823		
BR 2003014132	A	20050628	BR 2003-14132	20030922
EP 1546122	A1	20050629	EP 2003-750599	20030922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688556	A	20051026	CN 2003-824514	20030922
JP 2006502178	T	20060119	JP 2004-537146	20030922
ZA 2005002159	A	20050921	ZA 2005-2159	20050315
IN 2005CN00421	A	20070427	IN 2005-CN421	20050318
MX 2005PA03140	A	20050622	MX 2005-PA3140	20050322
NO 2005001970	A	20050616	NO 2005-1970	20050422
US 2006069268	A1	20060330	US 2005-528323	20050505
IN 2007CN01210	A	20070831	IN 2007-CN1210	20070322

PRIORITY APPLN. INFO.:

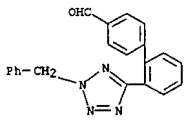
GB 2002-22056	A	20020923
WO 2003-EP10543	W	20030922
IN 2005-CN421	A3	20050318

OTHER SOURCE(S): MARPAT 140:287711
AB A process for the manufacture of valsartan is reported. Thus, L-valine was treated with 2'-(1H-tetrazol-5-yl)biphenyl-4-carboxaldehyde to give the imine which was reduced with NaBH4 and acylated with BuCOCl.
IT 151052-37-8 676129-97-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the manufacture of valsartan)
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)

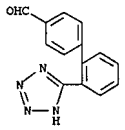
L22 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 676129-97-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(phenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



IT 151052-40-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the manufacture of valsartan)
RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

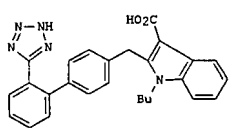
L22 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:1006744 CAPLUS
DOCUMENT NUMBER: 124:176118
TITLE: Process for preparing 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid via coupling of metalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde
INVENTOR(S): Fisher, Lawrence E.; Flippin, Lee A.; Martin, Michael G.
PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5468867	A	19951121	US 1994-250129	19940527
CA 2191575	A1	19951207	CA 1995-2191575	19950526
WO 9532961	A1	19951207	WO 1995-US6431	19950526
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526071	A	19951221	AU 1995-26071	19950526
ZA 9504305	A	19961126	ZA 1995-4305	19950526
EP 760814	A1	19970312	EP 1995-920592	19950526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1149294	A	19970507	CN 1995-193256	19950526
CN 1070491	B	20010905		
BR 9507900	A	19970916	BR 1995-7900	19950526
JP 10501229	T	19980203	JP 1995-500981	19950526
IL 113877	A	19981227	IL 1995-113877	19950526

PRIORITY APPLN. INFO.:

US 1994-250129	A	19940527
WO 1995-US6431	W	19950526

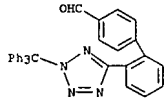
OTHER SOURCE(S): CASREACT 124:176118; MARPAT 124:176118
GI



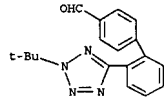
I

AB A process is claimed for the preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid (I) which process

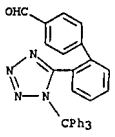
L22 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
comprises: (A) (i) treating 1-butyl-1H-indole-3-carboxylic acid with an organometallic base to give 2-metalated 1-butyl-1H-indole-3-carboxylic acid, (ii) optionally treating the 2-metalated 1-butyl-1H-indole-3-carboxylic acid with a metal halide to give 2-transmetalated 1-butyl-1H-indole-3-carboxylic acid and (iii) reacting the 2-metalated or 2-transmetalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-yl(hydroxy)methyl]-1H-indole-3-carboxylic acid; (B) dehydroxylating to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)-biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid and (C) deprotecting. Thus, e.g., treatment of 1-butyl-3-indolecarboxylic acid (217 g, 1.56 mol, prepn. given) with BuLi followed by 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]biphenyl-4-carbaldehyde (292 g, 0.956 mol, prepn. given) afforded 1-butyl-2-(2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]biphenyl-4-yl(hydroxy)methyl)-1H-indole-3-carboxylic acid (395.2 g, 0.56 mol); hydrogenation of the latter over 10% Pd/C afforded I (1.2 g, 2.66 mmol).
IT 138804-35-0P 151052-37-8P 155983-56-5P 165670-62-2P 174001-62-8P 174001-63-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid via coupling of metalated 1-butyl-1H-indole-3-carboxylic acid with protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carbaldehyde)
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



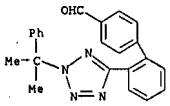
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



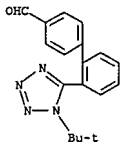
RN 155983-56-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



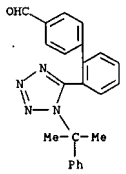
RN 165670-62-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



RN 174001-62-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(1,1-dimethylethyl)-1H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



RN 174001-63-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(1-methyl-1-phenylethyl)-1H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



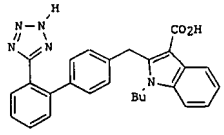
L22 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:608022 CAPLUS
DOCUMENT NUMBER: 123:112067
TITLE: Processes for preparing 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol
INVENTOR(S): Clark, Robin D.; Fisher, Lawrence E.; Flippin, Lee A.; Martin, Michael G.; Stabler, Stephen R.
PATENT ASSIGNEE(S): Syntex (U.S.A.) Inc., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5412102	A	19950502	US 1994-250397	19940527
US 5446121	A	19950829	US 1995-373677	19950117
US 5527918	A	19960618	US 1995-440040	19950512
CA 2191576	A1	19951207	CA 1995-2191576	19950526
WO 9532962	A1	19951207	WO 1995-US6432	19950526
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526439	A	19951221	AU 1995-26439	19950526
ZA 9504306	A	19961126	ZA 1995-4306	19950526
EP 760815	A1	19970312	EP 1995-921335	19950526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1149293	A	19970507	CN 1995-193255	19950526
CN 1070193	B	20010829		
BR 9507771	A	19970819	BR 1995-7771	19950526
JP 10501230	T	19980203	JP 1996-500982	19950526
IL 131709	A	20010430	IL 1995-131709	19950526
IL 113876	A	20010826	IL 1995-113876	19950526

PRIORITY APPLN. INFO.: US 1994-250397 A3 19940527
US 1995-373677 A3 19950117
IL 1995-113876 A3 19950526
WO 1995-US6432 W 19950526

OTHER SOURCE(S): CASREACT 123:112067; MARPAT 123:112067
GI

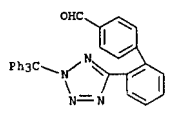


I

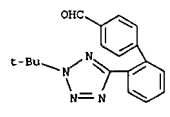
AB The preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid (I) comprises: (A) (i) treating protected 5-phenyl-2H-tetrazole, (ii) optionally treating the ortho-metalated protected 5-phenyl-2H-tetrazole with a metal halide to give ortho-transmetalated protected 5-phenyl-2H-tetrazole, (iii) reacting the ortho-metalated or ortho-transmetalated protected 5-phenyl-2H-tetrazole, optionally in the presence of phosphinated nickel or palladium catalyst, with 4-XC6H4CO2R1 in which X is halo and R1 is (C1-4)alkyl, to give protected 2'- (2H-tetrazol-5-yl) biphenyl-4-carboxylic acid (C1-4) alkyl ester, (iv) reducing the protected 2'-(2H-tetrazol-5-yl)biphenyl-4-carboxylic acid (C1-4)alkyl ester to give protected 2'-(2H-tetrazol-5-yl)biphenyl-4-methanol, and (v) halogenating the protected 2'-(2H-tetrazol-5-yl)biphenyl-4-methanol to give protected 4-halomethyl-2'-(2H-tetrazol-5-yl) biphenyl; (B) reacting the protected 4-halomethyl-2'-(2H-tetrazol-5-yl)biphenyl, optionally in the presence of phosphinated nickel or palladium catalyst, with 2-metalated or 2-transmetalated 1-but-1-yl-1H-indole-3-carboxylic acid to give protected 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid; and (C) deprotecting. Thus, e.g., treatment of protected I [1-butyl-2-(2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]-biphenyl-4-ylmethyl)-1H-indole-3-carboxylic acid, 8.0 g, 0.0141 mol, preparation given] with pentaerythritol tetrakis(2-mercaptoacetate) (4.84 mL, 0.0155 mol) and boron trifluoride etherate (6.92 mL, 0.056 mol) in 120 mL MeCN at room temperature for 1.5 h afforded I (5.9 g, 0.0131 mol).

IT 138804-35-0P 151052-37-8P 165670-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-butyl-2-[2'-(2H-tetrazol-5-yl)biphenyl-4-ylmethyl]-1H-indole-3-carboxylic acid involving deprotection of protected tetrazole with a Lewis acid in presence of a thiol)

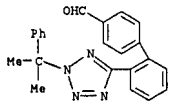
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



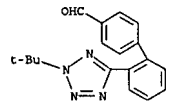
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



L22 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 165670-62-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1-methyl-1-phenylethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



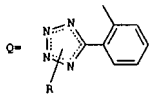
L22 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L22 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:305901 CAPLUS
DOCUMENT NUMBER: 122:187788
TITLE: Triarylborane derivatives, their preparation and their use as synthesis intermediates
INVENTOR(S): Chekroun, Isaac; Rossey, Guy; Magnat, Michel
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

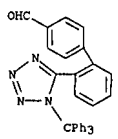
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5374735	A	19941220	US 1993-166026	19931214
FR 2712887	A1	19950602	FR 1993-14152	19931126
FR 2712887	B1	19951229		
US 5405960	A	19950411	US 1994-288192	19940809
EP 655452	A1	19950531	EP 1994-402641	19941121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2136668	A1	19950527	CA 1994-2136668	19941125
FI 9405561	A	19950527	FI 1994-5561	19941125
JP 07188252	A	19950725	JP 1994-291258	19941125
IL 111770	A	19980816	IL 1994-111770	19941125

PRIORITY APPLN. INFO.: FR 1993-14152 A 19931126
US 1993-166026 A3 19931214
OTHER SOURCE(S): CASREACT 122:187788; MARPAT 122:187788
GI



AB Triarylborane derivs. Q3B in which R either represents a group CR1R2R3 where R1, R2 and R3 are each, independently of one another, a (C1-C2)alkyl or aryl group, or represents a group CH2OR4 where R4 is a (C1-C2)alkyl or benzyl group, or represents a group SiR35 where R5 is a (C1-C2)alkyl or aryl group, R being in the 1 or 2 position of the tetrazole ring, were prepared by treating QLi with a trialkyl borate or trihaloborane. Q3B are synthetic intermediates for the synthesis of compds. which are angiotensin II antagonists.
IT 151052-37-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)

L22 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:227811 CAPLUS
DOCUMENT NUMBER: 122:105706
TITLE: Discovery of nonpeptide, potent conformationally restricted angiotensin II receptor antagonists
AUTHOR(S): Huang, Horng-Chih; Chamberlain, Timothy S.; Olins, Gillian M.; Corpus, Valerie M.; Chen, Susan T.; McMahon, Ellen G.; Palomo, Maria A.; Blaine, Edward H.; Manning, Robert E.
CORPORATE SOURCE: Depts. Chemistry and Cardiovascular Diseases Research, Searle R&D, St. Louis, MO, 63198, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(21), 2591-6
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of potent, selective, conformationally restricted angiotensin II (AII) receptor antagonists has been discovered. Two classes of conformationally restricted analogs were prepared: triazolone-based and imidazole-based biphenyl derivs. The most active compound, an imidazole-based analog, has an IC50 of 11 nM and a pA2 of 8.8.
IT 155983-56-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of conformationally restricted angiotensin II receptor antagonists)
RN 155983-56-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



L22 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:534129 CAPLUS
DOCUMENT NUMBER: 121:134129
TITLE: Preparation of [(heterocyclylmethyl)biphenylyl]tetrazoles as angiotensin II receptor antagonist intermediates
INVENTOR(S): Lo, Young S.; Rossano, Lucius T.; Larsen, Robert D.; King, Anthony O.
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA; Merck and Co., Inc.
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. 5,130,439.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

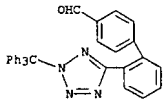
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5310928	A	19940510	US 1992-911812	19920710
US 5130439	A	19920714	US 1991-793514	19911118
WO 9310106	A1	19930527	WO 1992-US9979	19921118
W: AU, CA, CS, FI, JP, KR, NO, PL				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9331792	A	19930615	AU 1993-31792	19921118
AU 665388	B2	19960104		
EP 643704	A1	19950322	EP 1993-900550	19921118
EP 643704	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 08500323	T	19960116	JP 1992-509518	19921118
PL 171453	B1	19970430	PL 1992-303787	19921118
CA 2123900	C	19980714	CA 1992-2123900	19921118
CZ 283954	B6	19980715	CZ 1994-1205	19921118
PL 176124	B1	19990430	PL 1992-312131	19921118
SK 280887	B6	20000912	SK 1994-579	19921118
AT 250043	T	20031015	AT 1993-900550	19921118
EP 1384717	A2	20040128	EP 2003-18662	19921118
EP 1384717	A3	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
ES 2203614	T3	20040416	ES 1993-900550	19921118
FI 9402282	A	19940517	FI 1994-2282	19940517
FI 112945	B1	20040213		
NO 9401857	A	19940718	NO 1994-1857	19940518
NO 307932	B1	20000619		

PRIORITY APPLN. INFO.:

US 1991-793514	A2	19911118
US 1992-911812	A	19920710
US 1992-911813	A	19920710
EP 1993-900550	A3	19921118
WO 1992-US9979	A	19921118

OTHER SOURCE(S): MARPAT 121:134129
AB QZR [Q = WL; L = bond, (CH2)1-4, etc.; W = heterocyclyl, heteroaryl; R = 5-tetrazolyl substituted with CPh3, CMe3, Ph, etc.; Z = C6H4C6H4] were prepared by coupling of R1aR1bBC6H4R [R1a,R1b = Cl, Br, alkoxy, OH; R1aR1b = OC6H4O, O(CH2)2-4O] with QC6H4X (X = Br, iodo, OSO2R1; R1 = Me, F, C6H4Me, CF3). Thus, 2-butyl-4-chloro-5-hydroxymethyl-1-(p-bromobenzyl)-1H-imidazole was coupled with 2-(2-triphenylmethyl-2H-tetrazol-5-yl)phenylboronic acid (preparation each given) to give 2-butyl-4-chloro-1-[[2'-(2-triphenylmethyl-2H-tetrazol-5-yl)-1,1'-biphenyl-4-yl]methyl]-1H-imidazole-5-methanol.
IT 138804-35-0P

L22 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as angiotensin II receptor antagonist intermediate)
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



L22 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:508806 CAPLUS
DOCUMENT NUMBER: 121:108806
TITLE: Preparation of N-biphenylylmethyl-2-pyridone-4-carboxylates as angiotensin II antagonists
INVENTOR(S): Dressel, Juergen; Fey, Peter; Hanko, Rudolf; Huebsch, Walter; Kraemer, Thomas; Mueller, Ulrich E.; Mueller-Gliemann, Matthias; Beuck, Martin; Kazda, Stanislav; et al.
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

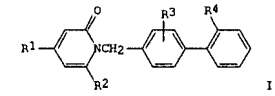
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 594019	A1	19940427	EP 1993-116404	19931011
EP 594019	B1	20000223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4319041	A1	19940428	DE 1993-4319041	19930608
AU 9347541	A	19940505	AU 1993-47541	19930922
AU 670315	B2	19960711		
NO 9303591	A	19940425	NO 1993-3591	19931007
AT 189893	T	20000315	AT 1993-116404	19931011
ES 2145021	T3	20000701	ES 1993-116404	19931011
PT 594019	T	20000831	PT 1993-116404	19931011
CA 2108814	A1	19940424	CA 1993-2108814	19931020
IL 107333	A	19980104	IL 1993-107333	19931020
CZ 283482	B6	19980415	CZ 1993-2217	19931020
FI 9304646	A	19940424	FI 1993-4646	19931021
PL 176171	B1	19990430	PL 1993-300803	19931021
ZA 9307853	A	19940519	ZA 1993-7853	19931022
CN 1089260	A	19940713	CN 1993-118766	19931022
CN 1040435	B	19981028		
JP 06199838	A	19940719	JP 1993-286167	19931022
HU 65819	A2	19940728	HU 1993-2997	19931022
RU 2118956	C1	19980920	RU 1993-48151	19931022
SK 279675	B6	19990211	SK 1993-1169	19931022
US 5596006	A	19970121	US 1995-368252	19950103
US 5863930	A	19990126	US 1995-574082	19951218
GR 3033207	T3	20000831	GR 2000-400901	20000412

PRIORITY APPLN. INFO.:

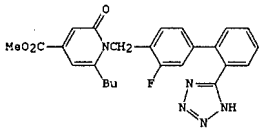
DE 1992-4235933	A	19921023
DE 1993-4319041	A	19930608
DE 1992-4235943	A	19921023
US 1993-137661	B1	19931015
US 1995-368252	A3	19950103

OTHER SOURCE(S): MARPAT 121:108806
GI

L22 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

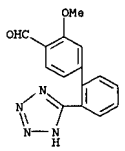


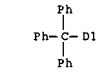
I



II

AB Title compds. (I; R1 = CO2H or alkoxycarbonyl; R2 = alkyl; R3 = halo, OH, cyano, alkyl, alkoxy, etc.; R4 = CO2H, tetrazolyl) were prepared as angiotensin II antagonists (no data). Thus, 2-(MeO)C6H4CO2H was amidated by H2NCMe2CH2OH and the cyclized product coupled with 3,4-FMeC6H3Br to give, after hydrolysis, 3,4-FMeC6H3C6H4(CN)-2 which was converted in 3 steps to 3,4-FMeC6H3C6H4R4-2 (R4 = triphenylmethyltetrazol-5-yl). The latter was condensed with 6-butyl-4-methoxycarbonyl-2-oxo-1,2-dihydropyridine to give, after deprotection, title compound II.
IT 156704-16-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of angiotensin II antagonist)
RN 156704-16-4 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 3-methoxy-2'-[(triphenylmethyl)-1H(or 2H)-tetrazol-5-yl]- (9CI) (CA INDEX NAME)





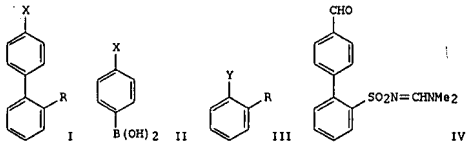
L22 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L22 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:508219 CAPLUS
DOCUMENT NUMBER: 121:108219
TITLE: Method for the preparation of biphenyl derivatives.
INVENTOR(S): Wagner, Adalbert; Bhatnagar, Neerja; Buendia, Jean; Griffoul, Christine
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 606065	A1	19940713	EP 1994-100048	19940104
EP 606065	B1	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 06234690	A	19940823	JP 1993-333929	19931228
JP 3586288	B2	20041110		
CA 2112795	A1	19940707	CA 1994-2112795	19940104
FI 9400032	A	19940707	FI 1994-32	19940104
NO 9400023	A	19940707	NO 1994-23	19940104
AU 9453029	A	19940714	AU 1994-53029	19940104
AU 677247	B2	19970417		
BR 9400018	A	19940726	BR 1994-18	19940104
ZA 9400018	A	19940818	ZA 1994-18	19940104
CN 1096511	A	19941221	CN 1994-100164	19940104
HU 67406	A2	19950428	HU 1994-18	19940104
AT 183732	T	19990915	AT 1994-100048	19940104
ES 2136669	T3	19991201	ES 1994-100048	19940104
US 5618975	A	19970408	US 1995-449396	19950524
US 5633400	A	19970527	US 1995-449389	19950524
GR 3031852	T3	20000229	GR 1999-402946	19991117
PRIORITY APPLN. INFO.:			DE 1993-4300137 A	19930106
			US 1994-177314 B3	19940104

OTHER SOURCE(S): CASREACT 121:108219; MARPAT 121:108219
GI

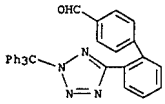


AB Title compds. [I; X = (protected) formyl; R = group inert to the reaction conditions of the synthesis], were prepared by reaction of phenylboronic acids II with halocarenes III (Y = halo). Thus, a mixture of 2-BrC6H4SO2N:CHNMe2, Ph3P, Na2CO3, Pd(OAc)2, PhMe, and H2O at 60° was treated with 4-OHCC6H4B(OH)2 (preparation given) in EtOH and the mixture was refluxed 3.5 h to give 83% title compound IV. I are intermediates for

L22 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

angiotensin II antagonists.

IT 138804-35-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via coupling of phenylboronic acid derivative with halocarene)
RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)

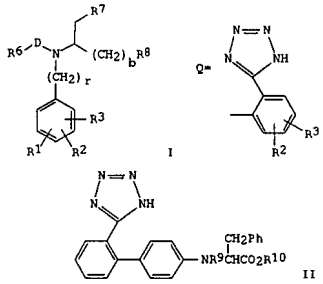


L22 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:457992 CAPLUS
DOCUMENT NUMBER: 121:57992
TITLE: Preparation of angiotensin II receptor blocking tertiary amides
INVENTOR(S): Markwalder, Jay A.; Pottorf, Richard S.
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5260325	A	19931109	US 1991-747022	19910819
PRIORITY APPLN. INFO.:			US 1991-747022	19910819

OTHER SOURCE(S): MARPAT 121:57992
GI



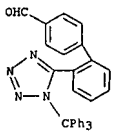
AB Amino acid N-[(tetrazolylbiphenylyl)methyl]amides and analogs [I; R1 = Q which is other than in the ortho position; R2, R3 = H, halo, alkyl, alkoxy, alkoxyalkyl; ; R5 = H, (cyclo)alkyl, alkenyl, alkynyl; R6 = (cyclo)alkyl, -alkenyl, alkynyl, cycloalkylalkyl, -alkenyl, -alkynyl, CH2CH2Z2(CH2)mR5 (Z = O, S, optionally substituted NH; m = 1-5), (un)substituted PhCH2; R7 = (cyclo)alkyl, perfluoroalkyl, acyl, aryl, alkylaryl, (CH2)nS(O)gCH2Ph (wherein n = 0,1; g = 0-2; Ph is optionally substituted), CH2S(O)gMe; R8 = CO2H, SO3H, P(O)(OH)2, or esters thereof, CHO, CH2OH, CH2O2C(CH2)nCO2H, cyano; D = CO, CS, SO2; b, g = 0-2; n = 0,1; r = 1,2], which is useful for treating hypertension and congestive heart failure, are prepared Thus, H-Phe-OMe3.HCl was suspended in EtOAc and treated with aqueous NaHCO3 to give the free amino acid which was alkylated by 2'-(N-triphenylmethyltetrazol-5-yl)-4-bromomethylbiphenyl in THF containing Et3N to give a phenylalanine derivative [(S)-II; R9 = H, R10 = CMe3]. The latter compound was acylated by valeryl chloride in DMF containing (Me2CH)2NEt

L22 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
and deprotected by aq. 95% CF3CO2H to give (S)-II (R9 = valeryl, R10 = H). A total of 13 I were prepd. and showed IC50 of <10 μM for antagonizing the binding of [125I]angiotensin II to a angiotensin II receptor prepn. from rat adrenal cortex.

IT 155983-56-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as intermediate for angiotensin II antagonist)

RN 155983-56-5 CAPLUS

CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[1-(triphenylmethyl)-1H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



L22 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:323851 CAPLUS

DOCUMENT NUMBER: 120:323851

TITLE: Preparation of 2-(tert-butyltetrazolyl)benzeneboronic acids and their coupling reactions to give 2-(tert-butyltetrazolyl)biphenyl derivatives

INVENTOR(S): Chekroun, Isaac; Bedoya, Zurita Manuel; Ruiz-Montes, Jose; Rossey, Guy

PATENT ASSIGNEE(S): Synthelabo S. A., Fr.

SOURCE: Fr. Demande, 9 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2688507	A1	19930917	FR 1992-3114	19920316
EP 561663	A1	19930922	EP 1993-400545	19930303

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: FR 1992-3114 A 19920316

OTHER SOURCE(S): CASREACT 120:323851; MARPAT 120:323851

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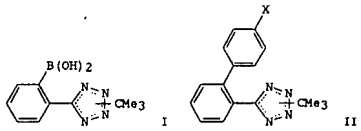


I II

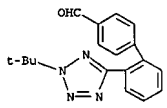
AB Title benzeneboronic acids I (1- or 2-substituted tetrazolyl) are prepared by protection of the tetrazole ring in 5-phenyltetrazole with a tert-Bu group, subsequent treatment of the product with an alkyllithium, reaction of the organolithium formed with a trialkyl borate, followed by acid hydrolysis. Compds. I are used for the preparation of tetrazolylbiphenyl derivs. II [X = C1-4 alkyl, C1-3 alkoxy, CH(OR5)2 or CH(OH)OR5 (R5 = H, C1-3 alkyl), or CH(OR5)2 forms a 1,3-dioxolane or 1,3-dioxane ring, or X = various substituted oxopyrimidinylmethyl groups]. Thus, 2-(1,1-dimethylethyl)-5-phenyl-2H-tetrazole (preparation given) was reacted with BuLi in THF, then B(OEt)3 was added, and the product was hydrolyzed with 10% HCl(aq) to afford I (2-substituted tetrazolyl) (III) in 71% yield. Reaction of III with 4-BrC6H4CHO in toluene with palladium dibenzylideneacetone/PPh3 catalyst and 2M NaZCO3 afforded II (X = CHO) in 70% yield.

IT 151052-37-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 151052-37-8 CAPLUS

CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)

L22 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L22 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:270807 CAPLUS

DOCUMENT NUMBER: 120:270807

TITLE: Derivatives of benzeneborinic acid, preparation thereof and use thereof as synthetic intermediates

INVENTOR(S): Chekroun, Isaac; Ruiz-Montes, Jose; Bedoya-Zurita, Manuel; Rossey, Guy

PATENT ASSIGNEE(S): Synthelabo S. A., Fr.

SOURCE: U.S., 3 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5278312	A	19940111	US 1992-967908	19921029
FR 2696746	A1	19940415	FR 1992-12166	19921012
FR 2696746	B1	19941118		
EP 593332	A1	19940420	EP 1993-402424	19931004
EP 593332	B1	19980114		

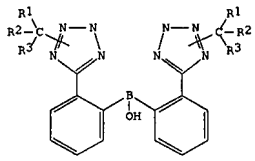
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

AT 162192	T	19980115	AT 1993-402424	19931004
FI 9304468	A	19940413	FI 1993-4468	19931011
IL 107242	A	19981030	IL 1993-107242	19931011
CA 2108231	A1	19940413	CA 1993-2108231	19931012
JP 06192240	A	19940712	JP 1993-254129	19931012
US 5382672	A	19950117	US 1993-155170	19931119

PRIORITY APPLN. INFO.: FR 1992-12166 A 19921012
US 1992-967908 A3 19921029

OTHER SOURCE(S): MARPAT 120:270807

GI



I

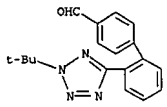
AB A process for the preparation of derivs. of benzeneborinic acid corresponding to the formula I in which R1, R2 and R3 represent, each independently of the others, either a (C1-C2)alkyl group or an aryl group, the group -CR1R2R3 being in position 1 or 2 of the tetrazole ring and method of use as synthetic intermediates.

IT 151052-37-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 151052-37-8 CAPLUS

CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)

L22 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L22 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

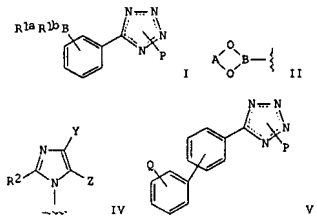
ACCESSION NUMBER: 1993:671389 CAPLUS
DOCUMENT NUMBER: 119:271389
TITLE: Tetrazolylphenylboronic acid intermediates for the synthesis of angiotensin II receptor antagonists
INVENTOR(S): Lo, Young Sek; Rossano, Lucius Thomas; Larsen, Robert D.; King, Anthony O.
PATENT ASSIGNEE(S): du Pont de Nemours, E. I., and Co., USA; Merck and Co., Inc.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9310106	A1	19930527	WO 1992-US9979	19921118
W: AU, CA, CS, FI, JP, KR, NO, PL				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5130439	A	19920714	US 1991-793514	19911118
US 5206374	A	19930427	US 1992-911813	19920710
US 5310928	A	19940510	US 1992-911812	19920710
AU 9331792	A	19930615	AU 1993-31792	19921118
AU 665388	B2	19960104		
EP 643704	A1	19950322	EP 1993-900550	19921118
EP 643704	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 08500323	T	19960116	JP 1992-509518	19921118
PL 171453	B1	19970430	PL 1992-303787	19921118
PL 176124	B1	19990430	PL 1992-312131	19921118
SK 280887	B6	20000912	SK 1994-579	19921118
AT 250043	T	20031015	AT 1993-900550	19921118
FI 9402282	A	19940517	FI 1994-2282	19940517
FI 112945	B1	20040213		
NO 9401857	A	19940718	NO 1994-1857	19940518
NO 307932	B1	20000619		

PRIORITY APPLN. INFO.:
US 1991-793514 A 19911118
US 1992-911812 A 19920710
US 1992-911813 A 19920710
WO 1992-US9979 A 19921118

OTHER SOURCE(S): CASREACT 119:271389; MARPAT 119:271389
GI

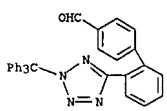
L22 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



AB Title compds. I [P = Ph3C, Me3C, C1-4-alkoxymethyl, MeSCH2, Ph-C1-4-alkoxymethyl, p-MeOC6H4CH2, 2,4,6-trimethylbenzyl, 2-(trimethylsilyl)ethyl, tetrahydropyranyl, piperonyl, benzenesulfonyl; R1a, R1b = independently Cl, Br, C1-4-alkoxy, OH; or R1aBR1b = II, A = Ph (sic) or (CH2)n, n = 2-4] were prepared as intermediates for the synthesis of angiotensin II receptor antagonists. Thus, reaction of B(OCHMe2)3 with the Li salt of 5-phenyl-2-trityltetrazole carbanion (generated from 5-phenyl-2-trityltetrazole and BuLi), followed by AcOH/H2O hydrolysis, afforded title compound I (P = 2'-Ph3C, R1a = R1b= OH) (III). More advanced intermediates that are precursors for angiotensin II receptor antagonists are prepared by cross-coupling of I with QC6H4X [X = Br, I, methanesulfonyloxy, toluenesulfonyloxy, fluorosulfonyloxy, trifluoromethanesulfonyloxy; Q = H, Me, C1-4-alkyl, hydroxymethyl, triorganosiloxymethyl, hydroxy-C1-4-alkyl, formyl, C1-4-acyl, C1-4-alkoxycarbonyl, WL [L = single bond, (CH2)t, t = 1-4, (CH2)rO(CH2)r, (CH2)rSOr(CH2)r, r = 0-2] and W = IV (R2 = C1-4-alkyl, Y = e.g., C1-4-alkyl, Z = e.g., hydroxymethyl)] in presence of metal catalyst, base, and coupling solvent to afford biphenyls V. Coupling of III with QC6H4X [X = 4-Br; Q = WL [L = CH2, W = IV (R2 = Bu, Y = Cl, Z = CH2OH)]] with catalyst formed from Pd chloride, Ph3P, and P(OCHMe2)3 afforded the corresponding V in 90% yield.

IT 138804-35-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(formation and reduction of, in preparation of angiotensin II receptor antagonist intermediates)

RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



L22 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L22 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:671171 CAPLUS
DOCUMENT NUMBER: 119:271171
TITLE: Preparation of 2-(5-tetrazolyl)biphenyls
INVENTOR(S): Daumas, Marc; Hoornaert, Christian; Chekroun, Isaac; Bedoya-Zurita, Manuel; Ruiz-Montes, Jose; Greciet, Helene; Rossey, Guy
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 550313	A1	19930707	EP 1992-403477	19921218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2685697	A1	19930702	FR 1991-16290	19911230
FR 2685697	B1	19940204		
FR 2688503	A1	19930917	FR 1992-3113	19920316
JP 05271205	A	19931019	JP 1992-348558	19921228
CA 2086364	A1	19930701	CA 1992-2086364	19921229
US 5371233	A	19941206	US 1992-998055	19921229
PRIORITY APPLN. INFO.:			FR 1991-16290 A	19911230
			FR 1992-3113 A	19920316
OTHER SOURCE(S):	MARPAT 119:271171			

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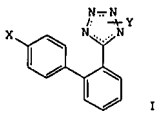


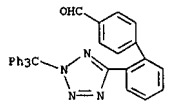
I

AB Title compds. {I; X = CHBr2, CHO, alkyl, CH(OR5)2, CH(OH)BR5; R5 = H, alkyl, etc.; Y = H, CMe3, CPh3, SnMe3, etc.; dashed line indicates optional position of double bonds} were prepared Thus, 4-BrC6H4Me was condensed with 5-(2-iodophenyl)-2-triphenylmethyl-2H-tetrazole and the product brominated to give I (X = CHBr2, Y = 2-CPh3).

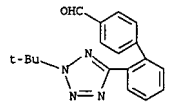
IT 138804-35-0P 151052-37-8P 151052-40-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)

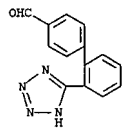
L22 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 151052-37-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(1,1-dimethylethyl)-2H-tetrazol-5-yl]- (9CI) (CA INDEX NAME)



RN 151052-40-3 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-(2H-tetrazol-5-yl)- (CA INDEX NAME)



L22 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:612716 CAPLUS
DOCUMENT NUMBER: 117:212716
TITLE: Preparation of tetrazolylphenylboronic acid intermediates for the synthesis of angiotensin II receptor antagonists
INVENTOR(S): Lo, Young S.; Rossano, Lucius T.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5130439	A	19920714	US 1991-793514	19911118
US 5206374	A	19930427	US 1992-911813	19920710
US 5310928	A	19940510	US 1992-911812	19920710
WO 9310106	A1	19930527	WO 1992-US9979	19921118
W: AU, CA, CS, FI, JP, KR, NO, PL				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9331792	A	19930615	AU 1993-31792	19921118
AU 665388	B2	19960104		
EP 643704	A1	19950322	EP 1993-900550	19921118
EP 643704	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 08500323	T	19960116	JP 1992-509518	19921118
CA 2123900	C	19980714	CA 1992-2123900	19921118
CZ 283954	B6	19980715	CZ 1994-1205	19921118
SK 280887	B6	20000912	SK 1994-579	19921118
AT 250043	T	20031015	AT 1993-900550	19921118
EP 1384717	A2	20040128	EP 2003-18662	19921118
EP 1384717	A3	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
ES 2203614	T3	20040416	ES 1993-900550	19921118
FI 9402282	A	19940517	FI 1994-2282	19940517
FI 112945	B1	20040213		
NO 9401857	A	19940718	NO 1994-1857	19940518
NO 307932	B1	20000619		
PRIORITY APPLN. INFO.:			US 1991-793514 A3	19911118
			US 1992-911812 A	19920710
			US 1992-911813 A	19920710
			EP 1993-900550 A3	19921118
			WO 1992-US9979 A	19921118
OTHER SOURCE(S):	MARPAT 117:212716			

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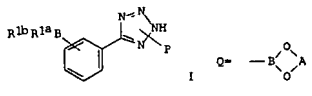


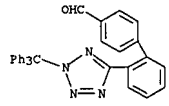
I

AB Title compds. I [P = Ph3C, Me3C, C1-4 alkoxymethyl, MeSCH2, Ph-C1-4-alkoxymethyl, 4-(MeO)C6H4CH2, 2,4,6-Me3C6H2CH2, CH2CH2(SiMe3),

L22 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
tetrahydropyranyl, piperonyl, PhSO2; R1a, R1b = Br, Cl, C1-4 alkoxy, HO; R1aR1bB = Q wherein A = Ph, (CH2)n wherein n = 2-4] are prepd. as angiotensin II receptor antagonist intermediates. 5-Phenyltetrazole, Et3N and Ph3CCl were reacted to give 5-phenyl-2-trityltetrazole which was treated with BuLi in heptane followed by (Me2CH)3BO3 to give I (P = 2-Ph3C, R1a = R1a = HO).

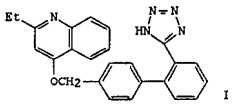
IT 138804-35-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



L22 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:612398 CAPLUS
DOCUMENT NUMBER: 117:212398
TITLE: New nonpeptide angiotensin II receptor antagonists. 2. Synthesis, biological properties, and structure-activity relationships of 2-alkyl-4-(biphenylylmethoxy)quinoline derivatives
AUTHOR(S): Bradbury, Robert H.; Allott, Christopher P.; Dennis, Michael; Fisher, Eric; Major, John S.; Masek, Brian B.; Oldham, Alec A.; Pearce, Robert J.; Rankine, Neil; et al.
CORPORATE SOURCE: Dep. Chem., ICI Pharm., Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Journal of Medicinal Chemistry (1992), 35(22), 4027-38
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:212398
GI

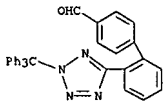


I

AB A novel series of title compds. was prepared When evaluated in an in vitro binding assay using a guinea pig adrenal membrane preparation, compds. in this series generally gave ED50 values in the range 0.01-1 μM. Structure-activity studies showed the quinoline N atom and a short alkyl chain at the quinoline 2-position to be essential for receptor binding. At 1-10 mg/kg in AII-infused, normotensive rats, the title compound I exhibited a dose-related inhibition of the pressor response with a good duration of action at the higher doses. In a renal hypertensive rat model, I showed a rapid and sustained lowering of blood pressure at a dose of 5 mg/kg.

IT 138804-35-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Grignard methylation of)

RN 138804-35-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)



L22 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L22 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:83555 CAPLUS
DOCUMENT NUMBER: 116:83555
TITLE: Preparation of quinoline derivatives, and their use as angiotensin II inhibitors
INVENTOR(S): Roberts, David Anthony; Bradbury, Robert Hugh; Pearce, Robert James; Thomas, Andrew Peter
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 456442	A1	19911113	EP 1991-304073		19910507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AU 9176285	A	19911114	AU 1991-76285		19910426
CA 2042126	A1	19911110	CA 1991-2042126		19910508
FI 9102220	A	19911110	FI 1991-2220		19910508
ZA 9103512	A	19920129	ZA 1991-3512		19910508
JP 04225959	A	19920814	JP 1991-104466		19910509
US 5369114	A	19941129	US 1993-101104		19930803
PRIORITY APPLN. INFO.:			GB 1990-10394	A	19900509
			US 1991-697145	B1	19910508

OTHER SOURCE(S): MARPAT 116:83555
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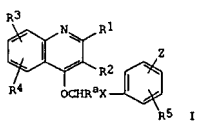

I

AB Title compds. I [R1 = H, C1-4 alkyl, C3-8 cycloalkyl, Ph, (substituted) C1-4 alkyl; R2 = H, C1-8 alkyl, C3-8 cycloalkyl, etc.; R3, R4 = H, C1-4 alkyl, C1-4 alkoxy, F-C1-4-alkoxy, halo, F3C, NC, O2N, HO, etc.; R3R4 = C1-4 alkylenedioxy attached to adjacent C of benzene moiety; R5 = H, C1-4 alkyl, C1-4 alkoxy, halo, F3C, NC, O2N; Ra = (substituted) C1-4, alkyl; X = substituted phenylene; Z = 1H-tetrazol-1-yl, CONH-1H-tetrazol-5-yl, etc.] or a salt thereof, are prepared I are of value in treating congestive heart failure (no data) and hypertension. Concentrated HCl was added to 2-methyl-4-[1-[2-(2-trityl-2H-tetrazol-5-yl)biphenyl-4-yl]ethoxy]quinoline (preparation given) in a mixture of EtOH and MeOH and left for 3 h to give I (R1 = Me, R2 = R3 = R4 = R5 = H, Ra = Me, X = C6H4, Z = 1H-tetrazol-5-yl).HCl (II). In vitro the IC50 of II against angiotensin II was 4 + 10-8M and in vivo against angiotensin II pressor response the ED50 was 0.18 mg/kg, i.v. Pharmaceutical formulations comprising I are given.

IT 138804-35-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and addition of methyllithium to)

RN 138804-35-0 CAPLUS

L22 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CN [1,1'-Biphenyl]-4-carboxaldehyde, 2'-[2-(triphenylmethyl)-2H-tetrazol-5-yl]- (CA INDEX NAME)